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Name: Peggy Nichols

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**IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCES**

In re Application for:

Oxana Ibraghimov-Beskrovnaya, et al.

Serial No.: 09/830,506

Filing Date: August 10, 2001

For: COMPOSITIONS AND METHODS
FOR TREATING POLYCYSTIC
KIDNEY DISEASE

Examiner: Haddad, Maher H.

Group Art Unit: 1644

APPELLANTS' BRIEF ON APPEAL

Mail Stop Appeal Brief

Commissioner for Patents

P.O. Box 1450

Alexandria, VA 22313-1450

Dear Sir:

On September 12, 2003, the U.S. Patent and Trademark Office issued a Final Office Action in connection with the above-identified application. On March 12, 2004, a Notice of Appeal and authorization to pay the appropriate fee were filed. In view of the filing of the Notice and payment of the fee, Appellant's Brief on Appeal was due May 12, 2004. Enclosed is a Petition for a Five month Extension of Time making the new due date October 12, 2004. Accordingly, this Brief is timely filed.

In accordance with 37 C.F.R. § 1.192(a) this Brief, along with Exhibits and, are filed in triplicate and are accompanied by the required fee.

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I. REAL PARTY IN INTEREST

The real party in interest is Genzyme Corporation. The subject patent application was assigned from the inventors to Genzyme Corporation on June 14, 2001 and June 15, 2001. The assignment was recorded in the U.S. Patent and Trademark Office on August 8, 2001, at Reel 012068, Frame 0559.

II. RELATED APPEALS AND INTERFERENCES

There are currently no other known appeals or interferences that may directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

Claims 1-13 and 15-29 are pending in the application; however, claims 1-22, 24-27 and 29 stand withdrawn from further consideration by the Examiner, 37 C.F.R. § 1.142(b), as allegedly drawn to non-elected inventions. The claims were misnumbered as filed, so a claim number "14" was not filed.

Claims 23 and 28 stand finally rejected. The addition of new claim 30 is respectfully requested.

A copy of the finally rejected Claims on Appeal is attached hereto as Exhibit A.

A complete Listing of the Claims is attached hereto as Exhibit B.

IV. STATUS OF THE AMENDMENTS

One claim has been added subsequent to the Final rejection. This appeal is taken on the basis of claims 23 and 28 as finally rejected, with the addition of new claim 30. A copy of claims 23, 28 and 30 is attached as Exhibit A to this paper.

V. SUMMARY OF THE INVENTION

The invention provides a method for modulating cell-cell adhesion in a suitable tissue by delivering to the tissue an effective amount of an agent that modulates the binding of polycystin in the tissue. (Page 7, lines 12 -15; page 9, line 3 to page 10, line 8; page 24, lines 3-10; page 42, line 23 to page 47, line 26; and page 57, line 21 to page 58, line 12). As described in the specification, a “suitable tissue” comprises a tissue wherein polycystin-1 and/or polycystin-2 is expressed. (Page 47, lines 7-9). Appellants provide specific examples of such tissue, which include kidney, liver, brain, neuronal cells, epithelial cells and astrocytoma cells. (Page 4, lines 15-24; page 8, lines 22-27; page 17, lines 23-24; and page 40, lines 25-28). The literature also has noted expression of polycystin in tissues such as the epithelial cells of pancreatic and mammary ducts, intestinal crypts, urothelium and bronchioles, basal keratinocytes of the skin, neural crest, brain, neural plexuses and adrenal medulla, myocardium vascular smooth muscle of elastic and distributive arteries and certain endothelial cells. (Page 4, lines 14-24).

The application provides numerous examples of agents that are useful for the practice of the claimed methods. “Agents” are intended to include a biological or chemical compound, a peptide, a protein, an antibody or an oligonucleotide. (See page 48, lines 17-28).

For example, the application sets forth amino acid sequences and polynucleotides encoding these sequence, wherein the amino acid sequences are immunogenic polypeptides present in the loop region of the transmembrane domain of polycystin. (See page 5, lines 19-26; page, 24 lines 22-30; and page 30, lines 8-16). Peptides for raising antibodies against an epitope outside the loop domain (e.g. Ig-like domain) also are provided, as well as the polynucleotide(s) encoding these peptides. (See page 5, lines 27-30 and page 30, lines 16-20). Further provided are antibodies that specifically bind to integral membrane proteins which has been correlated with polycystic kidney disease. (See page 6, lines 1-8). Ig-like domain peptides of polycystin, polynucleotides encoding them and antibodies raised against them are described by Appellants. (See page 6, lines 14-16; page 23, line 28 to page 24, line

10; page 30 lines 8-20; and page 52, line 1 to page 58, line 12). Recombinant polypeptides containing a fragment of a membrane-spanning segment of polycystin, methods of making them and antibodies raised against them are also provided. (See page 6, lines 17-25).

Variants and derivatives of these antibodies are taught. The antibodies can be polyclonal or monoclonal. (See page 18, lines 28-29; page 19, line 26 to page 27, line 13; page 21, line 21 to page 22, line 2) Hybridoma cell lines producing these antibodies are also provided. (See page 6, lines 13 and 14).

The antibodies are not limited to a specific species, i.e., they can be raised in various species, such as mouse, rat, rabbit or human. (See page 18, lines 27-30). They can be functional antibody fragments (see page 19, lines 6-18 and page 20; lines 7-13) chimeric antibodies (see page 19, lines 16-21), anti-idiotypic antibodies (see page 20, line 20 to page 21, line 12), or they can be linked to haptens, labels, beads and the like (see page 22, line 28 to page 23, line 17).

Many of the agents useful in the practice of this invention are polypeptides and polypeptide variants. (See page 7, line 21 to page 8, line 16; page 9, lines 2-19; page 57, line 21 to page 58, line 12; and Figures 1, 3, 4, 5, 6 and 12). In addition to the polypeptides described above, the application provides modified polypeptides having substitutions (see page 26, lines 21-30), post-translationally modified polypeptides (see page 26, lines 28 to 30), recombinant polypeptides produced in eukaryotic and prokaryotic systems (see page 7, lines 1-4; and page 36, line 28 to page 37, line 8,) and fusion proteins (see page 27, line 20 to page 28, line 5 and page 57, line 21 to page 28, line 12). Use of the peptides is described in detail in Appellants' specification, see, e.g., page 23, line 19 to page 25, line 30.

Polynucleotides encoding the polypeptides described above are also provided in the application papers. (See page 6, lines 28-30 and Figures 1, 3 and 4). The polynucleotides can increase or decrease polycystin expression and/or cell-cell or cell-matrix adhesion.

"Modulation" or "modulate" (see page 17, lines 11-12) of the interaction can be augmentation of adhesion (see page 47, line 6) or disruption of intercellular adhesion. (See page 9, line 26 to page 10, line 8; page 47, lines 5-7). Agents inhibit polycystin-1 mediated cell-cell

adhesion or cell-matrix adhesion include, for example antibodies that bind to the Ig-like domains of polycystin, polycystin fragments comprising these domains and agents that inhibit the expression of polycystin, e.g., antisense polynucleotides. (See page 47, lines 10-17 and page 48, line 20, see also Figure 14). Agents that augment cell-cell adhesion and/or cell-matrix adhesion include a polypeptide or other agent comprising the Ig-like domain of polycystin or full-length protein. (See page 47, lines 21 to 27). The polypeptides and proteins can be delivered as proteins or alternatively, as polynucleotides that are transcribed and translated *in vivo* to the active agent. (See page 47, lines 23-25; page 48, line 29 to page 49, line 18 and Figure 14). One can also restore normal cell-cell or cell-matrix adhesion in a tissue by removing any mutated soluble polycystin that may be interfering with normal intercellular processes. (See page 47, lines 24-27).

The agents can also be formulated for pharmaceutical delivery. (See page 50, lines 4-15; page 51, lines 3-25).

VI. ISSUES

- A. Whether Claims 23 and 28 Fail to Meet the Definiteness Requirement of 35 U.S.C. § 112, Second Paragraph?
- B. Whether the Specification Fail to Enable Claims 23 and 28?
- C. Whether the Specification Fails to Provide a Written Description for Claims 23 and 28?

VII. GROUPING OF CLAIMS

The claims on Appeal will not stand or fall together as they relate to the appealed issue. Claim 23 employs methods which augment and/or inhibit cell-cell or cell-matrix adhesion. Claim 28, depends on claim 23, but is specifically directed to augmentation. Therefore, the scope of claim 23 is broader than claim 28. Since some of the issues on appeal relate to enablement of the breadth of the claims, they should not stand or fall together.

VIII. ARGUMENTS

A. Claims 23 and 28 Meet the Definiteness Requirement of 35 U.S.C. § 112, Second Paragraph

1. The Office's Grounds for Rejection

The Office rejected claim 23 and dependent 28 under 35 U.S.C. § 112, second paragraph on the ground that the use of the term “suitable tissue” is indefinite. The Office’s ground for rejection was that while page 17, line 24 of the specification discloses the kidney, liver, brain and neuronal tissues to express PKD1 polypeptide, the metes and bounds of the claimed “suitable tissue” remains unknown.

The Office suggested that to overcome the rejection, claim 23 be amended to recited the language disclosed on page 47, lines 8-9 or to recite specific tissue as disclosed on page 17, line 24.

2. Appellants' Argument

Appellants first note that a claim is read in light of the specification, not in a vacuum. As explained in *S3 Inc. v. nVidia Corp.*, 259 F.3d 1364, 59 USPQ2d 1745 (Fed. Cir. 2001):

“The purpose of claims is not to explain the technology or how it works, but to state the legal boundaries of the patent grant. A claim is not ‘indefinite’ simply because it is hard to understand when viewed without benefit of the specification.”

Id. at 1369.

Appellants’ specification, on page 42, lines 6 to 9 states that:

“In another aspect, the modulation of cell-cell or cell-matrix adhesion is an increase or to enhance cell-cell or cell-matrix adhesion mediated by polycystin in a suitable tissue. As used herein, a “suitable tissue” includes any tissue which polycystin, i.e., polycystin-1 or polycystin-2, is expressed as been described above.”

Additional disclosure of “suitable tissue” includes, but is not limited to page 17, lines 18 to 24; page 24, lines 13 to 16 and page 47, lines 20 to 28. Thus one of skill in the art, upon reading Applicants’ disclosure at the time the application was filed, would have no

doubt as to the scope of the claims. For this reason, the rejection is in error and should therefore be reversed.

However, in a sincere effort to remove the ground for rejection under 35 U.S.C. § 112, second paragraph, Appellants request consideration and entry of new claim 30 which specifically identifies suitable tissue as suggested by the Office.

- B. The Specification Meets the Enablement Requirement of 35 U.S.C. § 112, First Paragraph
- C. The Specification Provides a Written Description for Claims 23 and 28 as required by 35 U.S.C. § 112, First Paragraph

Prior to specifically addressing the Office's rejections, Appellants note that page 4 of the Final Office Action indicated that the Office handled the Written Description rejection with the Enablement rejection, each for allegedly failing to comply with 35 U.S.C. § 112, first paragraph. The Office stated that therefore, a detailed rebuttal of Appellants' arguments under the Written Description Requirement was not separately provided.

For that reason, Appellants will present the following comments in reply to the Enablement and Written Description rejections, each under 35 U.S.C. § 112, first paragraph.

1. The Office's Grounds for Rejection

A. Enablement

The Office opined that the full scope of the claims was not enabled. The Office asserted that the specification only enables a method for enhancing cell-cell adhesion in a polycystin expressing tissue by delivering to the tissue an antibody against polycystin *in vitro*.

During the initial rebuttal to this rejection, Appellants' one ground for traversal was that the Office failed to meet its initial burden of providing a *prima facie* case.

The Office responded that Appellants' reply was not persuasive because in its opinion, the specification fails to provide a representative number of structurally related agents. The Office alleged that based on the teachings of the specification, one of skill in the art would not know the

identity of a reasonable number of representative agents falling within the scope of the instant claims and consequently would not have known how to make them.

In support of its position the Office pointed to *In re Fisher*, 166 USPQ 18 (CCPA 1970) to support the statement of law that the more unpredictable an area is, the more specific enablement is necessary in order to satisfy the statute. The Office noted that Appellants' specification does not show use of an animal as model system to enhance cell-cell adhesion. The Office also argued the Appellants' reliance on an *in vitro* model to disrupt cell-cell adhesion does not accurately reflect the relative efficacy of the claimed therapeutic strategy. The Office also alleged that specification does not adequately teach how to effectively reach any therapeutic endpoint in mammals by administering the therapeutic the antibody against polycystin. The Office also stated that the specification fails because it does not teach how to extrapolate data obtained from the *in vitro* model of disrupting cell-cell adhesion studies to the development of effective *in vivo* therapeutic treatment.

The Office also stated that in view of the lack of predictability of the art to which the invention pertains, the lack of established clinical protocols for effective cell adhesion-based therapies, undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in Appellants' specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for the promotion or enhancement of cell-cell or cell-matrix adhesion. The Office also alleged that there is insufficient guidance and direction in the specification for diseases or conditions that would be targeted with anti-polycystin antibody.

B. Written Description

The Office also rejected claims 23 and 28 under 35 U.S.C. 112, first paragraph, for allegedly failing to be supported by an adequate written description. The Office alleged that Appellants were not in possession of the full scope of the claims. The Office opined that the specification only supports a method for enhancing cell-cell adhesion in a polycystin expressing tissue by delivering to the tissue an antibody against polycystin *in vitro*.

2. Statement of the Law as Interpreted and Applied by the Courts

A. Enablement

The Federal Circuit succinctly stated the law of enablement in *National Recovery Technologies, Inc. v. Magnetic Separation Systems, Inc.*, 166 F.3d 1190, 1196 (Fed. Cir. 1999):

“The enablement requirement ensures that the public knowledge is enriched by the patent specification to a degree at least commensurate with the scope of the claims. The scope of the claims must be less than or equal to the scope of the enablement. The scope of enablement, in turn, is that which is disclosed in the specification plus the scope of what would be known to one of ordinary skill in the art without undue experimentation.”

Specific guidance for evaluating whether an application satisfies the enablement requirement was set forth by the court in *In re Wands*, 858 F.2d 731 (Fed. Cir. 1988). Eight factors by which an examiner or reviewing court can assess whether a disclosure is sufficient to enable one of ordinary skill in the art to practice a claimed invention throughout its scope without having to engage in undue experimentation were provided. They are: (1) the quantity of experimentation necessary; (2) the amount of direction or guidance presented; (3) the presence or absence of working examples; (4) the nature of the invention; (5) the state of the prior art; (6) the relative skill of those in the art; (7) the predictability or unpredictability of the art; and (8) the breadth of the claims. *In re Wands*, 858 F.2d at 737 (citing *Ex parte Forman*, 230 USPQ 546, 547 (Bd. Pat. App. & Int. 1986)).

The Wands Court also noted that “a considerable amount of experimentation is permissible, if it is merely routine, or if the specification in question provides a reasonable amount of guidance with respect to the direction in which the experimentation should proceed.” *Id.* at 737.

In addition, the courts have held that the Office should not necessarily limit an applicant’s claim scope only to those embodiments actually disclosed in the specification. Indeed, one can, in principle, support broad claims without even a single disclosed embodiment. *See Spectra-Physics Inc. v. Coherent Inc.*, 827 F.2d 1524 (Fed. Cir. 1987). The embodiment need not necessarily have even been reduced to practice. *See In re Wright*, 999 F.2d 1557, 1561

(Fed. Cir. 1993) (“Nothing more than objective enablement is required, and therefore it is irrelevant whether [a] teaching is provided through broad terminology or illustrative examples.”); *In re Robins*, 429 F.2d 452, 457 (CCPA 1970) (stating that “representative [samples] are not required by the statute and are not an end in themselves”); *In re Long*, 368 F.2d 892, 895 (CCPA 1966) (holding that the absence of a working example does not in and of itself compel the conclusion that a specification does not satisfy the requirements of section 112).

Moreover, when evaluating enablement, the evidence of record must be analyzed against the level of skill of the art at the time the application was filed. For example, in the early 1960s, the treatment of cancer was an alleged utility that appeared to be incredible in the light of the knowledge of the art. *In re Citron*, 325 F.2d 248 (CCPA 1964). However, only six years later, the Board remarked in *Ex parte Krepelka*, 231 USPQ 746, 747 (Bd. Pat. App. & Int. 1986),¹ that “[t]he state of the art of cancer treatment has advanced markedly since the time of the decision in *In re Citron*” and it was no longer considered an “incredible utility” Even more recently, the Federal Circuit remarking that “[m]odern science has previously identified numerous successful chemotherapeutic agents,” *In re Brana*, 51 F.3d 1560, 1566, 34 USPQ2d 1436, 1441 (Fed. Cir. 1995).

B. Written Description

The “Written Description” requirement of 35 U.S.C. § 112, first paragraph, ensures that the inventor had possession of the specific subject matter claimed, as of the filing date of the application. In *In re Edwards*, 568 F.2d 1349 (CCPA. 1978) the predecessor to the Federal Circuit articulated the function of the written description requirement, stating:

“[The f]unction of [the] description requirement is to ensure that the inventor had possession, as of the filing date of the application relied on, of the specific subject matter later claimed by him; to comply with the description requirement, it is not necessary that the application describe the claimed invention in *ipsis verbis*; all that is required is that it reasonably convey to persons skilled in the art that, as of

¹ Reversing the examiner’s rejection of claims to a broad genus of compounds having an alleged utility in the treatment of many types of cancer, the Board remarked that “[a]melioration of the symptoms or even cure of the disease is no longer considered to be ‘incredible’,” *Ex parte Krepelka*, 231 USPQ at 747, and, citing *Buting* for the proposition that “[s]ubstantiating evidence to support utility may be in the form of animal tests which constitute recognized screening procedures with clear relevance to utility in humans,” *Ex parte Krepelka*, 231 USPQ at 747, found applicants’ *in vitro* and animal tests clearly sufficient to withstand the examiner’s rejection. Once again, one sees how a later case turned the rationale in *Buting* on its head, in light of subsequent developments in the cancer art.

the filing date thereof, the inventor had possession of the subject matter later claimed by him.”

Id at 1351-52, 196 USPQ at 467 (citations omitted).

Additional courts have further expounded on the Written Description requirement. For example, the subject matter a claim need not be described literally or "in *ipsis verbis*" in order for the specification to satisfy the description requirement. *See, e.g., In re Lukach*, 442 F.2d 967, 969 (CCPA 1971). It should be sufficient that the specification "convey clearly to those skilled in the art the information that the applicant has invented the specific subject matter later claimed." *See, e.g., In re Wertheim*, 541 F.2d 257, 262 (CCPA 1976); *In re Ruschig*, 379 F.2d 990, 996 (CCPA 1967). Additionally, the Patent Office always has the burden of demonstrating that the applicant has failed to comply with the "written description" requirement. *See, e.g., In re Edwards*, 568 F.2d at 1356, *In re Wertheim*, 541 F.2d at 265.

3. Appellants' Rebuttal

The apparent grounds for the Office's rejection of the claims for allegedly failing to be enabled by the specification are: 1) that the specification has failed to provide a reasonable number of experimental examples to support the breadth of the claim term "agent", i.e. that the specification fails to "provide a reasonable number of structurally related agents. The artisan would not know the identity of a reasonable number of representative agents falling within the scope of the instant claims." (see page 3 of the Final Office Action); and 2) that the evidence of usefulness would not enable one of skill in the art to practice the claimed invention, due to the unpredictability in moving from the *in vitro* tests disclosed in Appellants' specification to *in vivo* use.

First Appellants again reassert that the Office has failed to meet its burden of providing a *prima facie* case of enablement. The subject application was filed in 2001, and claims priority to three provisional applications filed during the course of 1998 and 1999. In the first Office Action, (see page 3 of the Office Action issued November 20, 2002) the Office provided a 1994 research article published at least 4 years prior to the earliest priority date claimed, to support its statements regarding the level of skill and the unpredictability in the art of antibody therapy.

Appellants maintain that this reference published 4 years prior to the effective filing date cannot describe the state of the art at the time the priority applications were filed (in 1998 or 1999) and therefore cannot be used to rebut Appellants' specification and evidence of record. Additionally, the Office has not provided any evidence that the general statements regarding the use of antibodies, directed against a different therapeutic target, is relevant to the claimed invention. Moreover, the Office provided no evidence with respect to the use of agents other than antibodies in practice of the claimed invention, e.g., polypeptides and oligonucleotides.

Appellants have attempted set out for the Board in the Summary of Invention section of this paper the detail and scope of the specification as it was filed. With respect to support for the scope of the claim term "agents", Appellants' specification provides sequence information and working examples of the use of proteins, polypeptides, oligonucleotides, polyclonal antibodies and monoclonal antibodies that modulate (claim 23) cell-cell and cell-matrix interactions. With respect to claim 28, Appellants provide a detailed description and examples of agents that promote or enhance cell-cell or cell-matrix adhesion. As stated above:

Agents that augment cell-cell adhesion and/or cell-matrix adhesion include a polypeptide or other agent comprising the Ig-like domain of polycystin or full-length protein. (See page 47, lines 21 to 27). The polypeptides and proteins can be delivered as proteins or alternatively, as polynucleotides that are transcribed and translated *in vivo* to the active agent. (See page 47, lines 23-25; page 48, line 29 to page 49, line 18). One can also restore normal cell-cell or cell-matrix adhesion in a tissue by removing any mutated soluble polycystin that may be interfering with normal intercellular processes. (See page 47, lines 24-27).

Appellants maintain that the level of skill in the art at the time the invention was made, in combination the Appellants' specification, enables the full scope of the term "agent."

In rebuttal to the Office's arguments that the specification does not adequately teach how to effectively reach any therapeutic endpoint in mammals by administering the therapeutic antibody against polycystin nor teach how to extrapolate data obtained from *in vitro* model of disrupt cell-cell adhesion studies to the development of effective *in vivo* therapeutic treatment, commensurate in scope with the claimed invention, Appellants direct the Office's attention to

page 42, line 23 to page 57, line 30 of the specification. These portions of the specification teach how to make and use agents for their claimed purpose(s) and provides, a comparison of the *in vitro* efficacy of several of the agents against the known interaction of p53 and SV40 large T antigen. (See page 45, lines 15 to 20). Moreover, Appellants maintain that the Office has failed to provide any evidence that the teachings of the specification was evaluated as it pertains to one of skill in the art at the time the application was filed or its earliest priority date. In response to the Office's assertion that the specification does not provide guidance and direction for diseases or conditions for treatment by the claimed methods, Appellants direct the Office's attention to pages 2 and 3 of the specification.

Finally, with respect to the Written Description rejections, Appellants incorporate by reference the statements and evidence of record as described above, in particular the evidence of actual reduction to practice of numerous agents falling within the scope of the claims. Appellants maintain that their detailed specification establishes that they were in possession of the full scope of the invention at the time of its filing.

Reversal of the rejections under 35 U.S.C. § 112, first paragraph, is respectfully requested.

VIII. CONCLUSION

For the reasons provided herein, the rejections are in error and reversal is respectfully requested.

Respectfully submitted,

Date: Oct. 12, 2004

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EXHIBIT A

Claims on Appeal

23. (Original Claim) Method for modulating cell-cell adhesion in a suitable tissue, comprising delivering to the tissue an effective amount of an agent that modulates the binding of polycystin in the tissue.

28. (Previously Amended) The method of claim 23, wherein the modulation of cell-cell or cell-matrix adhesion is promotion or enhancement of cell-cell or cell-matrix adhesion in a suitable cell or tissue.

30. (New) The method of claims 23 or 28, wherein the suitable tissue comprises a tissue wherein polycystin-1 and/or polycystin-2 is expressed.

EXHIBIT B

Listing of the Claims

The following is a complete listing of the claims.

1. (Withdrawn) An isolated antibody or a fragment thereof that binds to an epitope present in the transmembrane domain of polycystin and specifically recognizes a polycystin-related polypeptide having an apparent molecular weight in the range of about 600 to about 800 kD.
2. (Withdrawn) An isolated antibody of claim 1, wherein the polypeptide has an apparent molecular weight of about 600 kD.
3. (Withdrawn) An isolated antibody of claim 1, wherein the polypeptide has an apparent molecular weight of about 800 kD.
4. (Withdrawn) An isolated antibody comprising an epitope, wherein the epitope comprises a peptide having amino acids as shown in Figure 1 (SEQ ID NO:2) selected from the group consisting of amino acid residues 2621 to 2710, amino acid residues 2734 to 3094, amino acid residues 3116 to 3300, amino acid residues 3364 to 3578, amino acid residues 3623 to 3688, amino acid residues 3710 to 3914, amino acid residues 3931 to 4046, amino acid residues 2166 to 2599, amino acid residues 4097 to 4302, amino acid residues 4148 to 4219, amino acid residues 4220 to 4302, amino acid residues 27 to 360, amino acid residues 843 to 1200, amino acid residues 1205 to 1625, and amino acid residues 1626 to 2136.
5. (Withdrawn) An isolated antibody or a fragment thereof that specifically binds to the transmembrane domain of an integral membrane protein that is associated with polycystic kidney disease, wherein the integral membrane protein also binds to a reference antibody selected from the group consisting of anti-FP-L1, anti-FP-L2, anti-FP-L3, anti-FP-L4, anti-FP-L5, anti-FP-L6, anti-FP-L7, anti-MAL-REJ antibody, anti-MAL-BD3 antibody, anti-FP-46-2 antibody, anti-FP-46-lc antibody, or anti-FP-LRR antibody.

6. (Withdrawn) An isolated antibody of any of claims 1 to 5, wherein the antibody is a polyclonal antibody.

7. (Withdrawn) An isolated antibody of any of claims 1 to 5, wherein the antibody is a monoclonal antibody.

8. (Withdrawn) An isolated antibody of any of claims 1 to 5 labeled with a detectable label.

9. (Withdrawn) A composition comprising a carrier and an antibody of any of claims 1 to 5.

10. (Withdrawn) A hybridoma cell line that produces the monoclonal antibody of claim 7.

11. (Withdrawn) An isolated antibody of any of claims 1 to 5, wherein the polypeptide or protein is expressed in a tissue selected from the group consisting of kidney, brain, liver and neuronal tissues.

12. (Withdrawn) A recombinant polypeptide comprising a polypeptide fragment of polycystin, wherein the fragment is a membrane-spanning segment of polycystin selected from the group consisting of loop 1, loop 2, loop 3, loop 4 and loop 7.

13. (Withdrawn) A recombinant polypeptide comprising a polypeptide fragment of polycystin, wherein the fragment comprises a peptide having amino acids as shown in Figure 1 (SEQ ID NO:2) selected from the group consisting of amino acid residues 2621 to 2710, amino acid residues 2734 to 3094, amino acid residues 3116 to 3300, amino acid residues 3364 to 3578, amino acid residues 3623 to 3688, amino acid residues 3710 to 3914, amino acid residues 3931 to 4046, amino acid residues 2166 to 2599, amino acid residues 4097 to 4302, amino acid residues 4148 to 4219, amino acid residues 4220 to 4302, amino acid residues 27 to 360, amino acid residues 843 to 1200, amino acid residues 1205 to 1625, and amino acid residues 1626 to 2136.

14.

15. (Withdrawn) A composition comprising a carrier and a polypeptide of claim 13.
16. (Withdrawn) An isolated polynucleotide encoding the recombinant polypeptide of claim 13.
17. (Withdrawn) A gene delivery vehicle comprising the polynucleotide of claim 16.
18. (Withdrawn) A host cell transformed with the isolated polynucleotide of claim 16.
19. (Withdrawn) An isolated polypeptide having an apparent molecular weight in the range of about 600 to about 800 kD that specifically binds to an antibody or fragment thereof of claim 1.
20. (Withdrawn) An isolated polypeptide of claim 19, wherein the polypeptide has an apparent molecular weight of about 600 kD.
21. (Withdrawn) The isolated polypeptide of claim 19, wherein the polypeptide has an apparent molecular weight of about 800 kD.
22. (Withdrawn) A diagnostic kit for detecting a polycystin-related polypeptide present in a sample, comprising an antibody of any of claims 1 to 5, and instructions for the use of the antibody to detect the polypeptide.
23. (Original Claim) Method for modulating cell-cell adhesion in a suitable tissue, comprising delivering to the tissue an effective amount of an agent that modulates the binding of polycystin in the tissue.
24. (Withdrawn) The method of claim 22, wherein the modulation of cell-cell or cell-matrix adhesion is a reduction of cell-cell or cell-matrix adhesion.
25. (Withdrawn) The method of claim 24, wherein the agent prevents or inhibits transcription and/or translation of a polycystin polypeptide in a cell.
26. (Withdrawn) The method of claim 24, wherein the agent is an antisense polynucleotide to an isolated polynucleotide of claim 16.
27. (Withdrawn) The method of claim 24, wherein the agent is a ribozyme that inhibits translation of a isolated polynucleotide of claim 16.

28. (Previously Amended) The method of claim 23, wherein the modulation of cell-cell or cell-matrix adhesion is promotion or enhancement of cell-cell or cell-matrix adhesion in a suitable cell or tissue.

29. (Withdrawn) The method of claim 28, wherein an effective amount of a polycystin Ig-like domain is delivered to the cell or tissue.

30. (New) The method of claims 23 or 28, wherein the suitable tissue comprises a tissue wherein polycystin-1 and/or polycystin-2 is expressed.